
Hua Medicine
华领医药

# 2021 Annual Results Presentation

March 2022

# Disclaimer

This document may contain statements that constitute “forward-looking statements”, including, but not limited to, statements relating to the implementation of strategic initiatives, and other statements relating to our future business development and economic performance.

While these forward-looking statements represent our judgments and future expectations concerning the development of our business, a number of risks, uncertainties and other statutory requirements may render actual developments and results to differ materially from our expectations.

These factors include, but are not limited to, (1) general market, macro-economy, governmental and regulatory trends, (2) movements in local and international securities markets, currency exchange rates and interest rates, (3) competitive pressures, (4) technological developments, (5) changes in the financial position or creditworthiness of our customers, partners, vendors obligors and counterparts, and changes in the developments in the markets in which they operate, (6) legislative or regulatory developments, (7) management changes and changes to our business group structure and (8) other key factors that may adversely affect our business and financial model.

We are not under any obligation to (and expressly disclaim any such obligations to) update or alter forward-looking statements whether as a result of new information, future events, or otherwise.

This material may not be reproduced, distributed or transmitted to any other person or incorporated in any way into another document or other material without the prior written consent of us.

This document is not:

(a) an offer of securities for sale in Hong Kong or elsewhere; or

(b) an invitation to enter into an agreement to acquire, dispose of, subscribe for or underwrite securities; or related to the issue of any securities.

**All documents and conference contents are for institutional investors, no unauthorized audio and video recordings and may not be directly or indirectly reproduced even modified, redistributed or forwarded to any other person and may not be published in whole or in part for any purpose.**

# Company Overview

# Commercialization of Dorzagliatin is Well on Track


- Dorzagliatin NDA was filed as a global **first-in-class** glucokinase modulator for Type 2 Diabetes in March 30, 2021 and accepted on April 23, 2021. As of November 23, 2021, all 6 technical reviews were successfully completed, with **potential approval by mid-year 2022**
  - Monotherapy for drug-naïve T2D patients
  - Add-on to metformin for metformin-tolerant T2D patients
- In collaboration with Bayer and key partners to actively prepare for commercialization
  - In Sep 2021, signed a supply chain strategic cooperation with Sinopharm
  - In Feb 2022, announced a supply agreement with WuXi STA for the commercial manufacturing of dorzagliatin
- The manufacturing factory at Lingang is under construction – the combination of self production and external procurement will ensure adequate dorzagliatin commercial supply

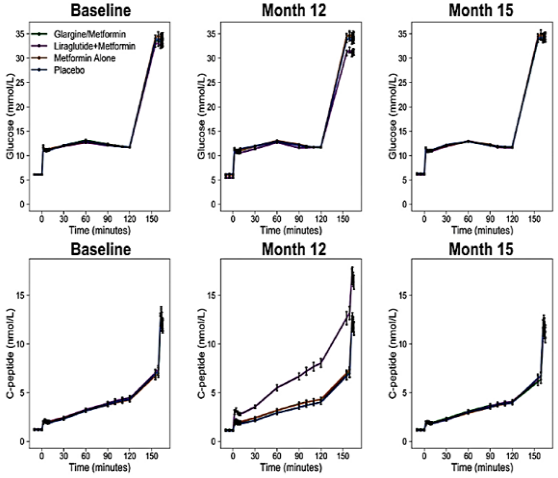
# Dorzagliatin – A differentiated first-in-class antidiabetic drug to advance diabetes treatment globally

- Global First-in-Class GK modulator Dorzagliatin for Type 2 Diabetes – monotherapy and in combination with metformin
- Commercial launch expected in 2022 in China
- Dorzagliatin improves glucose sensitivity and glucose stimulated early phase insulin secretion function to achieve effective glycemic control with good safety and tolerability
  - HMM0102-103 trials - Dorzagliatin improves early phase insulin secretion
  - HMM0201 trial - Dorzagliatin improves glucose disposition index
  - Phase 3 SEED, DAWN studies demonstrated the potential for best composite control rate in OAD for drug-naïve and metformin-tolerant T2D patients in China
  - DREAM study demonstrated 65% drug free diabetes remission for 12 month in T2D patients who achieved glycemic control with Dorzagliatin treatment in SEED study
  - SENSITIZE study demonstrated Dorzagliatin improves glucose sensitivity and 2$^{nd}$ phase insulin secretion which is impaired in MODY-2 patients
  - HMM111 trial - Dorzagliatin repairs GLP-1 secretion in T2D patients in US
  - HMM110 trial - Dorzagliatin can be used in all stage CKD subjects for glycemic control without dose adjustment

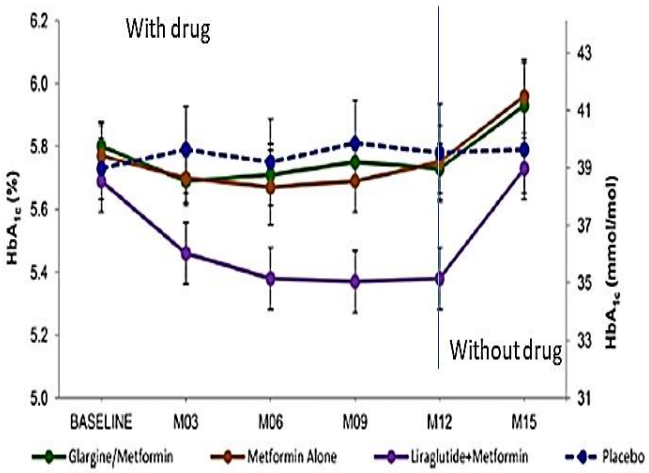
# Loss of GSIS function in β-cells is the root cause of T2D

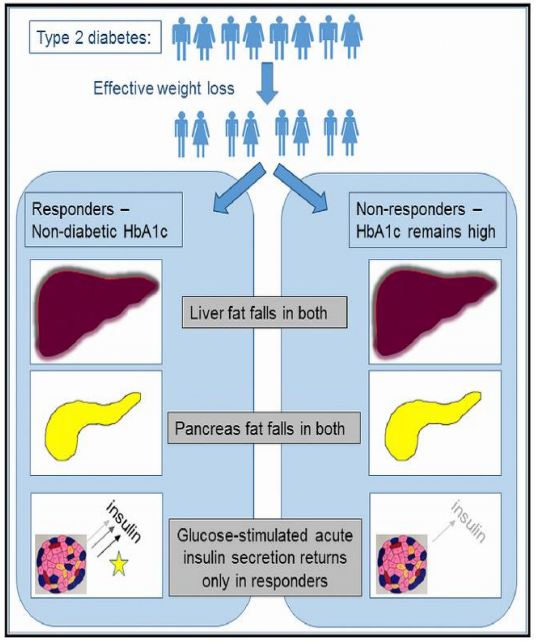
- **RISE Study**: Drug naive T2D and IGT subjects were treated for 12 month with **Metformin (Green), GLP-1 + Metformin (Red) and Glargine + Metformin (Purple)** did not show sustained improvement of beta cell function in 15 Month, 3 months after drug withdraw
- **DiRECT Study**: Weight loss driven diabetes remission is dependent on restoring glucose stimulated acute-insulin secretion. That is, through external factors (weight loss) affecting the root of the disease (glucose-stimulated early-phase insulin secretion) to promote remission

Lack of **insulin secretion** enhancement by leading T2D drugs




**Blood glucose well controlled** by drugs (A1c < 6.0) but not when drug withdrawn



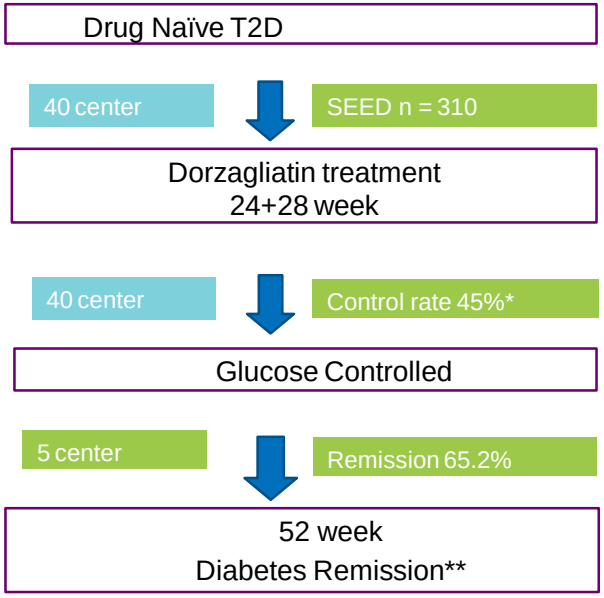



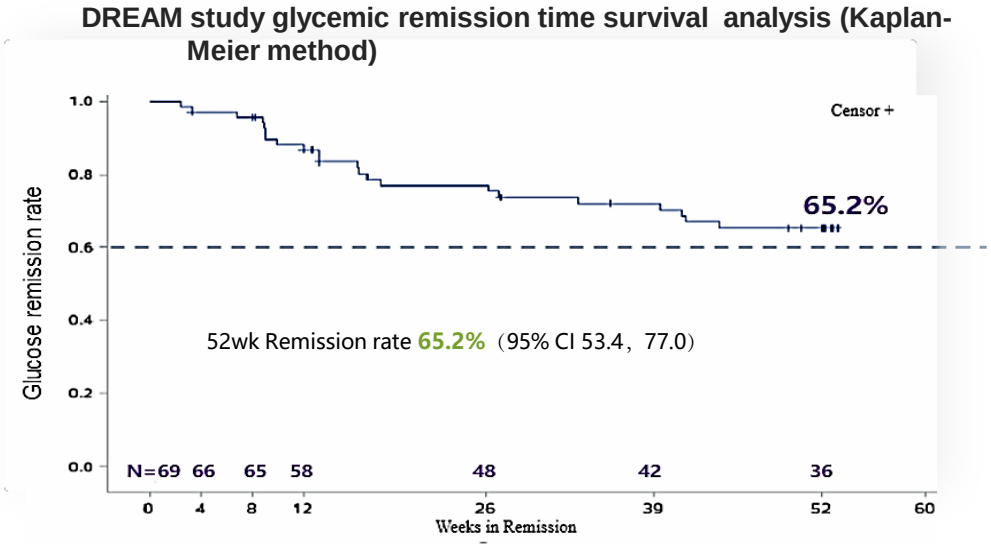

*source: RISE Consortium. Diabetes Care. 2019 Sep;42(9):1742-1751. DiRECT Cell Metabolism 2018;28:547-556*

# Dorzagliatin Effect in Diabetes Remission: DREAM Study

DREAM study: a diabetes remission in drug naïve patients who completed SEED study

- Total 69 subjects with average A1c of 6.61%, 2.2 year disease history
- Blood glucose are on target without any glucose lower drug
- 65.2% diabetes remission achieved at 52 week
- IIT study at 5 clinical centers in China



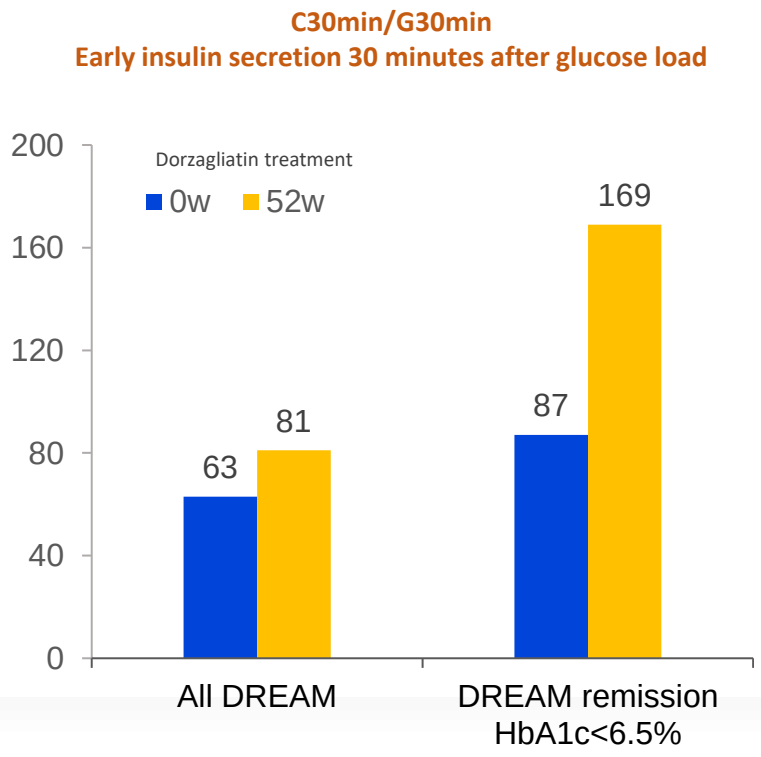



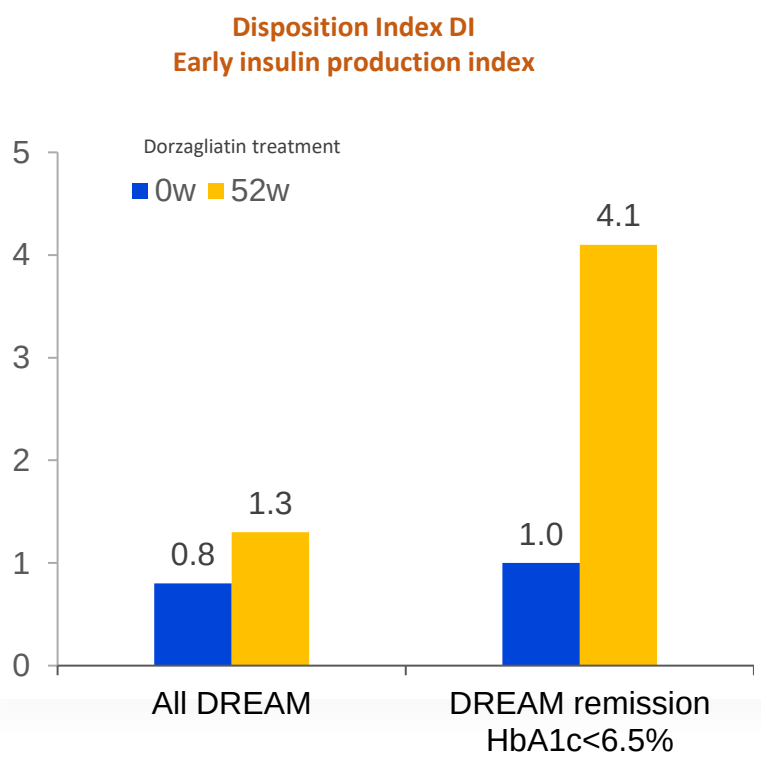

* Control rate at 24 week of SEED study: HbA1c < 7%

** Based on the 2021 "Expert Consensus on Diabetes Remission" (HbA1c lasting less than 6.5% within 3 months without medication), survival analysis showed that the remission rate at 12 weeks was **52.0%** (95% CI 31.2%, 69.2%)

# Improve early-phase insulin secretion, which is the core mechanism to achieve diabetes remission

After receiving dorzagliatin treatment, the improvement of early insulin secretion is more significant in the diabetes remission group (Data from SEED study)




Dorzagliatin is the only diabetes drug that directly hits the root of the disease, and some patients can still maintain the effect after stopping the drug!



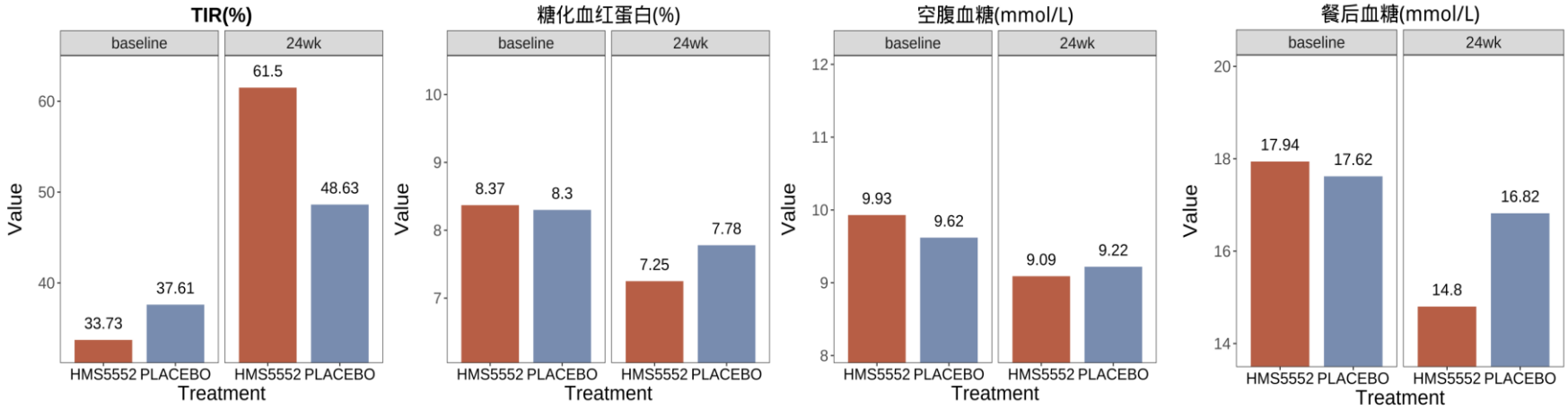


*Note: The results of all indicators in the figure are all medians*

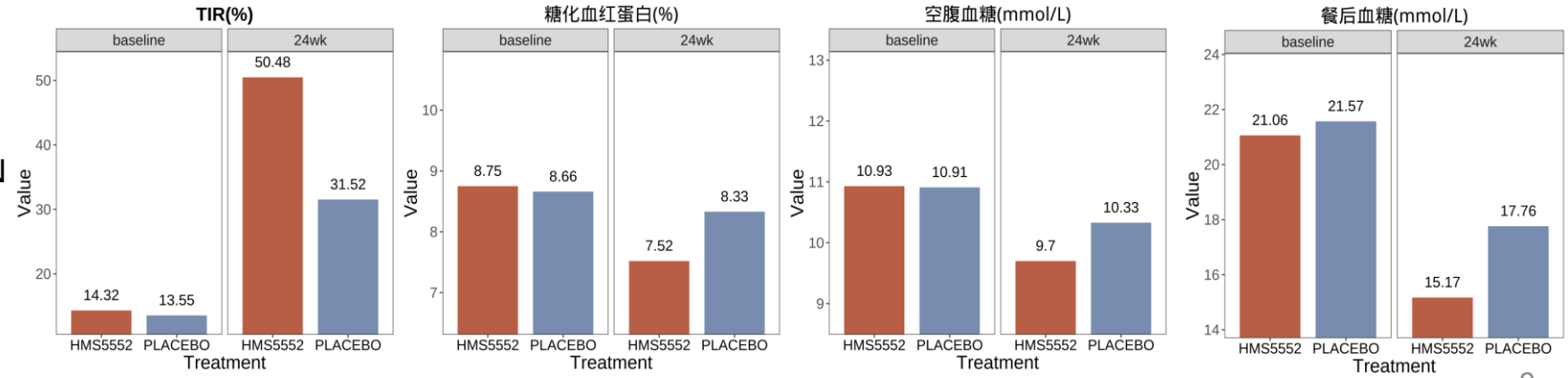
# Dorzagliatin significantly improves TIR for patient : preventing complications

- In two Phase III clinical trials of SEED and DAWN, patients with T2D_C subtype significantly reduced postprandial blood glucose and significantly increased TIR
- TIR (%) : Time In Range (%) Within 24 hours, the Time proportion of blood glucose In the healthy Range (%), TAR (%) Time proportion of blood glucose Above the healthy Range (%) and TBR (%) Time proportion of blood glucose Below the healthy Range (%) constitute dynamic blood glucose monitoring

SEED



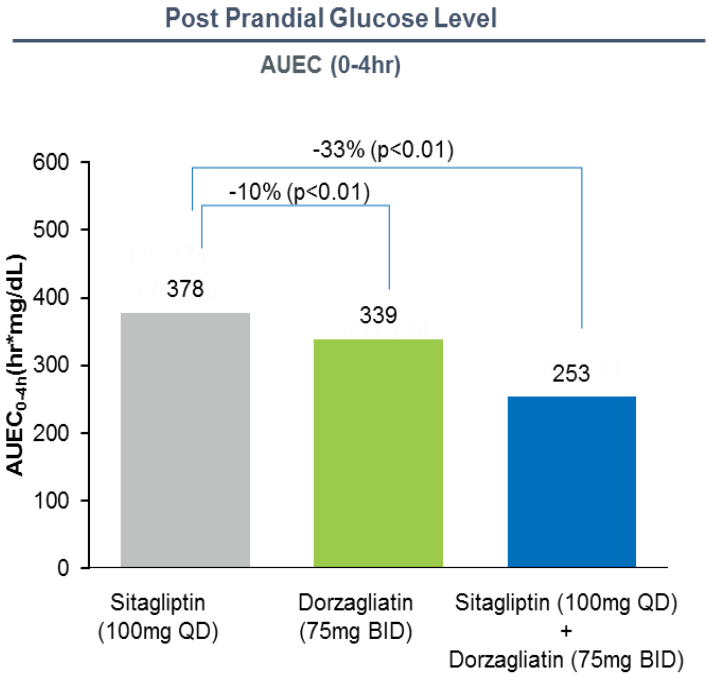

DAWN




**TIR value is calculated by Hua Medicine algorithm using clinical blood glucose index*

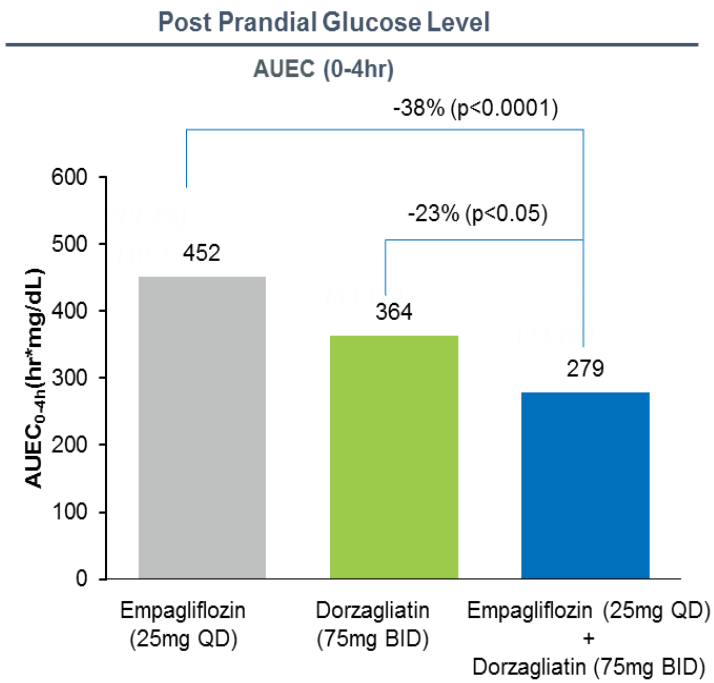
# Positive results with drug combination of dorzagliatin

Phase I clinical trials of dorzagliatin in combination with sitagliptin (DPP-4 inhibitor) and empagliflozin (SGLT-2 inhibitor) in the United States have shown synergistic results




**DPP-4 inhibitor:**

- ✓ US$ 4B global sales in 2019




**SGLT-2 inhibitor:**

- ✓ Fastest growing among OAD with US$ 6B global sales in 2019 and ~24% yoy growth

*Note: AUC represents area under the curve, while AUEC represents area under the effect curve.*

# Dorzagliatin has the potential to be the ONLY oral anti-T2D therapeutic for select DKD patients

| Drug use guidelines for T2D patients with diabetic kidney disease | | |
|---|---|---|
| Dorzagliatin |  | *Oral* |
| Metformin |  | |
| DPP-4 |  | |
| SGLT-2 |  | |
| GLP-1 |  | *Injectibles* |
| Insulin |  | |

 No dose adjustment required

 Dose adjustment required

 Contraindicated

- Patients with diabetic kidney disease make **up 20-40% of the total** T2D patient population globally
- In China, **patients with moderate, severe, and end-stage chronic kidney disease comprise 21.9%** of the T2D patients

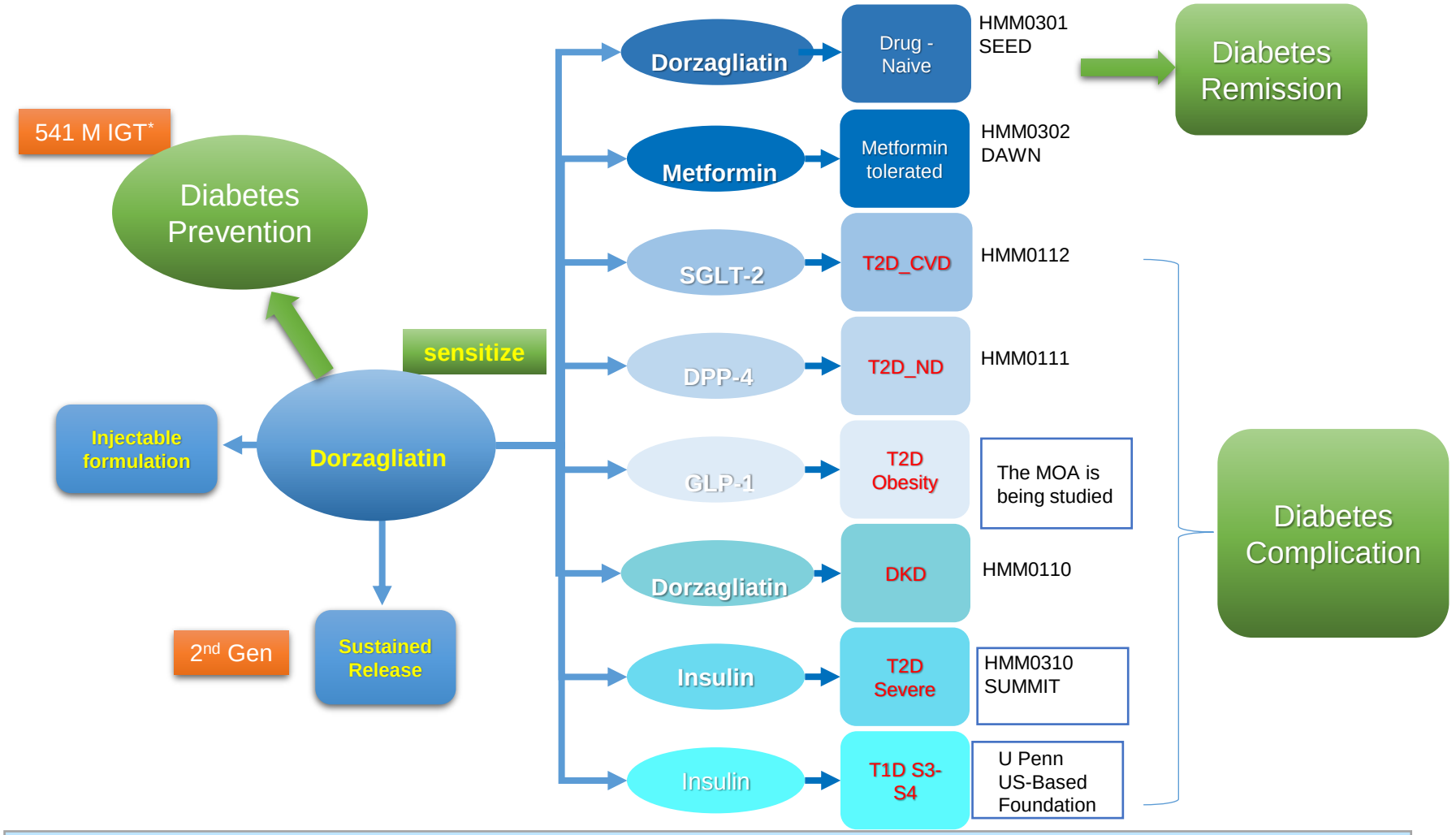
**Study:**

HMM0110 was conducted in China to evaluate whether dorzagliatin can be readily used in Type 2 diabetes (T2D) patients with impaired renal function.

**Conclusion:**

- In subjects with end stage renal disease and are not on dialysis, **the study indicated no significant impact on PK properties in subjects treated with dorzagliatin.**
- This result **supports dorzagliatin as a promising solution and potential supplementary option for T2D patients with moderate, severe and end stage chronic kidney disease** (i.e., stages 3-5 of CKD) which can **provide satisfactory blood glucose control safely and without dose adjustment**.

# Restore glucose homeostasis and advance diabetes care diabetes remission and ultimately prevention




- **Diabetes remission** by early intervention of Dorzagliatin: impact about 100 M diabetes patients
- **Diabetes prevention** by Dorzagliatin for IGT subjects: about 541 M IGT patients worldwide
- **Diabetes complication prevention** by early combination of Dorzagliatin: about 440 M T2D patients have one or more comorbidities





** IDF Diabetes Atlas 10th Edit; Leon Litwak Diabetology & Metabolic Syndrome 2013, 5: 57; Yuanyuan Cheng, Li Chen Global J Obesity, Diabetes and Metabolic Syndrome 2020, 7: 18*

# Hua Medicine exploratory research in human

- **Successful DREAM Study: Jianhua Ma, JE Zeng, SL Gan et al completed** [NCT0491854]
  - Evaluation of Diabetes Remission after dorzagliatin treatment
  - The DREAM Study, a 65.2% diabetes remission rate was observed without any antidiabetic medication during the 52-week research period, control rates of 45%

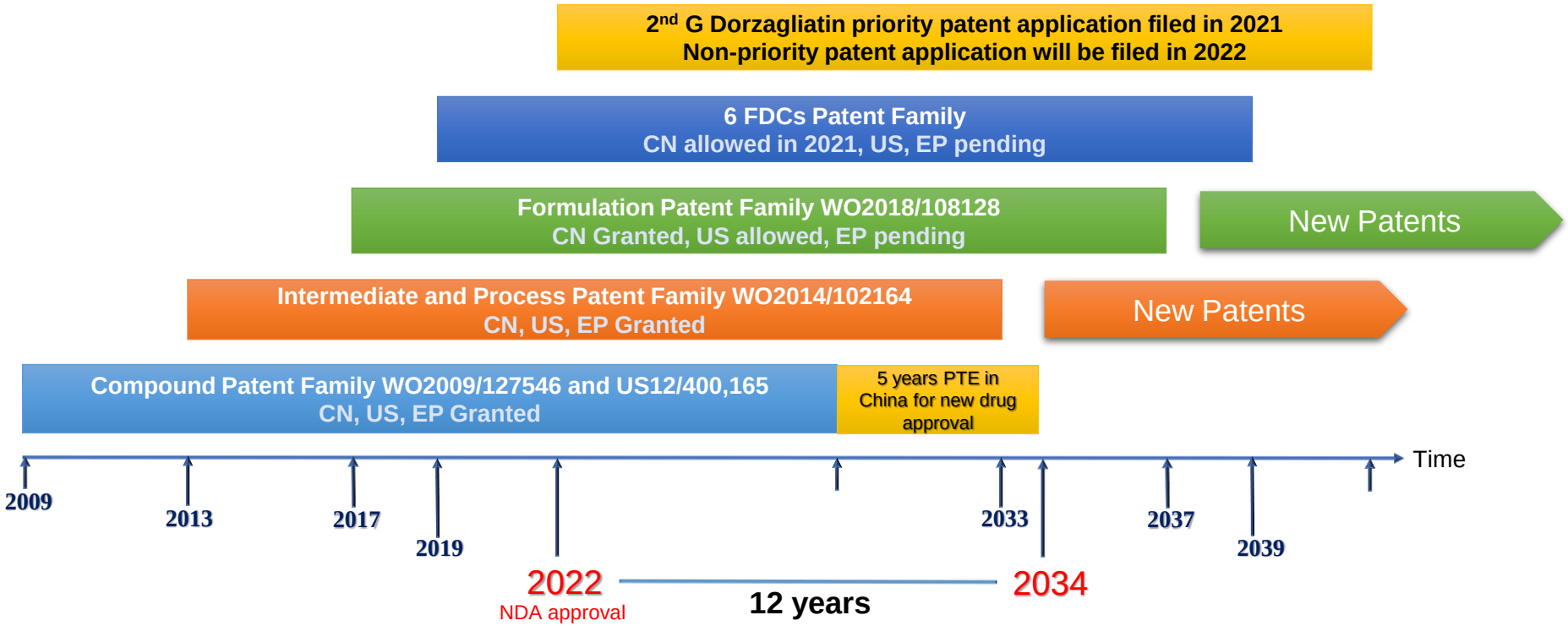
- **Successful SENSITIZE study: Julianna Chan, Elaine Chow et al in Hong Kong completed** [NCT04531631]
  - Evaluation of glucose sensitivity and insulin secretion improvement in MODY-2 and T2D subjects with single does treatment in a double blinded, placebo controlled cross over study
  - Dorzagliatin significantly improves β-cell glucose sensitivity and insulin secretion, ADA 2022 Report

- **Mechanism of action study: Rita Basu et al, NIH grant approved** [NCT05098470]
  - Effects of modulation of gluconeogenesis, glycogenolysis and glucokinase activity on endogenous glucose production in T2DM.
  - T2D patients randomized into metformin, Insulin glargine or dorzagliatin, and will be treated for 8 weeks. Studies at pre- and post treatment using triple tracer technology
  - Systematic understanding of the characteristics and functions of three core diabetes drugs in diabetes treatment

# Outlook in 2022

# Dorzagliatin Patent Portfolio

The Chinese patent for dorzagliatin is expected to be extended to 2034, and various global patents including the 2nd generation GKA are in urgent application and prosecution



# Dorzagliatin for T1D in the United States

- **There is a significant unmet medical need in the more than 1.6 million of T1D patients in the United States**
  - Limited treatment option: Insulin is the only treatment for T1D
  - ~80% of T1D patients in the US have a glycosylated hemoglobin (HbA1c) level above 7.0% and are at high risks of developing related micro- and macro-vascular complications
  - Glucose fluctuations are the biggest issue point in T1D management
  - TIR management has been introduced into Universal Health Care to reduce the risk of diabetic macrovascular and microvascular complications
- **The approach to T1D indication are separated into two projects**
  - **Stage 4 T1D** Program planned for initiation in 2022 – **improve glycemic control** and protect against hypoglycemia
    - Michael Rickels, MD, Professor and Medical Director of T1D Program at U Penn, is the leading PI for the study of dorzagliatin in the established T1D（Stage 4).
    - A dose ranging study (Ib) will be conducted as a pilot trial and define the doses for the phase II trial
  - **Stage 3 T1D** Program planned for initiation in 2022 – **preservation of beta-cell function**
    - Working with a leading US-based diabetes foundation, a trial in newly diagnosed T1D patient (Stage 3) is under design phase to evaluate the potential of Dorzagliatin in delaying or prevention of disease progression into stage 4 condition in a 12 month study

# Dorzagliatin business development strategy

Seek opportunities to continue to expand the development opportunities of dorzagliatin in the European, American and Japanese markets, Southeast Asian market and the "Belt and Road" market to realize the value of innovation.

- Partner with Bayer China and achieve commercial excellence in Diabetes Care
  - An innovative model to shape the Chinese diabetes market and management
  - Raising the standard of care and management of diabetes and related diseases

- Partner with local leader in China for drug development clinical opportunities for diabetes prevention, mitigation and elimination of complications
  - Opportunity in diabetes prevention in China and SE Asia (IGT population)

- Partner with local leader in US and EU for drug development and market entry with FDC (once a day tablet) and 2nd generation of dorzagliatin
  - Opportunity in T1D and T2D care in US
  - Opportunity in DKD care in US and EU
  - Opportunity in T2D partners in the Middle East and North Africa

# Financial Section

# Financial Summary

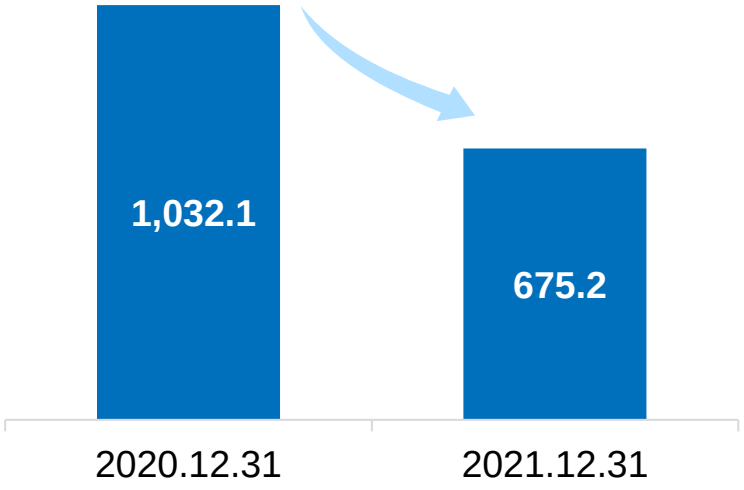
**Cash Balance:** RMB675.2 million of cash at 12/31/2021 vs. 1,032.1 million at 12/31/2020.

Total cash decrease of RMB356.9 million, consisted of

- Net cash used in operating activities was RMB273.0 million
- Net cash used in investing activities was RMB68.2 million
- Net cash used in financing activities was RMB6.2 million
- Net effect of exchange rate changes was RMB9.5 million

Net cash used in operation activities of RMB273.0 million mainly includes cash payment of RMB 159.9 million for the research and development activities and of RMB113.1 million for the administrative activities.

RMB' million



# Financial Summary- continued

**Loss before tax** of RMB325.7 million in the year of 2021 vs. RMB393.1 million in the year of 2020

**Research and development expenses** of RMB186.8 million in the year of 2021 vs. RMB221.0 million in the year of 2020

- a decrease of RMB57.8 million for dorzagliatin clinical trials, which was primarily attributable to decreased costs associated with the last patient out of the 52-week study period of SEED/HMM0301 in March 2020 and DAWN/HMM0302 in September 2020;
- an increase of RMB21.5 million in chemical, manufacturing, and control (CMC) expenses, which was primarily attributable to the chemical and process research for our fructose kinase inhibitor candidates and manufacture-dynamic process validation batch production for our NDA approval conducted in the year of 2021;
- a decrease of RMB12.1 million for labor costs, which was primarily attributable to a decrease of share-based payment under the accelerated amortization method.
- a decrease of RMB2.6 million for dorzagliatin licensing and patent fee, which was primarily attributable to a Patent Cooperation Treaty (PCT) application for the fixed-dosed combination associated with dorzagliatin in the year of 2020 and no such cost in the year of 2021;
- an increase of RMB17.2 million for others, which was primarily attributable to the allocation of rental fee, depreciation and amortization expense, property costs, utility cost and other cost related to our new headquarter which came into operation at the end of 2020.

# Financial Summary- continued

**Administrative expenses of** RMB134.8 million in the year of 2021 vs. RMB140.1 million in the year of 2020

- a decrease of RMB1.0 million in labor costs which was attributable to the decrease of RMB9.2 million in share-based payment under the accelerated amortization method, adjusted for an increase of RMB8.2 million in cash compensation;
- a decrease of RMB4.2 million in marketing and PR costs, mainly due to the digital program and national and regional congress conducted in the year of 2020 and less such cost in the year of 2021 under our marketing strategy;
- a decrease of RMB5.5 million in consulting fee, mainly associated with the commercialization strategy consulting and legal service to realize qualified collaboration with Bayer in the year of 2020 and no such cost in the year of 2021;
- adjusted for an increase of RMB4.7 million in depreciation and amortization expense, mainly due to the decoration and additional equipment purchased for our new headquarter.

Hua Medicine
华领医药